peared after 18 minutes of slow-wave sleep. Consecutively, a 56-minute cyclic alternating sleep pattern was recorded, interrupted by many short arousals and followed by a fourth REM period. After 12 minutes Ms. A woke up in panic from her "usual nightmare." At that time no signs of sleep paralysis or EEG abnormalities were present on polysomnography.

Despite considerable improvement after psychotherapy, Ms. A's nightmares continued. Cyproheptadine therapy was prescribed at up to 12 mg at 10:00 p.m. Her nightmares soon became less frightful, and they decreased to less than one a week. Her serum level of cyproheptadine 12 hours after intake of 12 mg was 6 μg/liter. A second polysomnography was conducted. Sleep latency was 10 minutes. Non-REM stage 2 and slow-wave sleep were interrupted by three arousals. The first REM period (13 minutes) occurred after 144 minutes of sleep, followed by slow-wave sleep with two periods showing a cyclic alternating sleep pattern. After 70 minutes REM sleep reappeared for 6 minutes. A final REM period lasted for 10 minutes after a light 5-minute sleep. No nightmares were reported.

The main differences between the two sleep recordings were the paucity of deep sleep during the first night and the percentages of REM sleep—30.4% and 12.6%, respectively (normal values=20%–25%) (5). Moreover, during the first polysomnography, REM sleep appeared earlier and more predominantly in the middle third of the night. The second polysomnography showed a nearly normal sleep architecture.

In accordance with earlier reports, it seems that cyproheptadine might be of considerable value in the treatment of posttraumatic nightmares.

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Posttraumatic Stress Disorder and Sleep Difficulty

To the Editor: Patients with posttraumatic stress disorder (PTSD) frequently report difficulty falling asleep, decreased sleep duration, and trauma-related nightmares. Effective pharmacotherapeutic treatments for these problems have not been identified. Open-label trials suggest that cyproheptadine may be a promising treatment (1, 2). Cyproheptadine acts as a histamine 1 (H_1) and serotonin 2 (5-HT_2) receptor antagonist. Evidence indicates that 5-HT_2 antagonists increase stages of slow-wave sleep without altering total sleep time (3) and improve sleep outcome (4).

We conducted a double-blind, randomized, placebo-controlled trial of cyproheptadine for treating sleep problems found in PTSD. The participants were male Vietnam veterans who had current combat-related PTSD according to the Clinician Administered PTSD Scale (5) and who also reported at least moderately severe nightmares on the Pittsburgh Sleep Quality Index (6). The exclusion criteria included current substance abuse, use of a selective serotonin reuptake inhibitor, mania or hypomania, and any medical condition that contraindicated the use of cyproheptadine. After complete description of the study to subjects, written informed consent was obtained. Sixty-nine subjects were enrolled in this 2-week trial across two sites. Posttreatment data on the Clinician Administered PTSD Scale, the Pittsburgh Sleep Quality Index, and a nightmare questionnaire were available for 60 subjects.

The drug and placebo groups did not differ at pretreatment on severity scores on the Clinician Administered PTSD Scale ($F=2.06$, $df=1, 56$, $p=0.16$), total scores on the Pittsburgh Sleep Quality Index ($F\approx0.00$, $df=1, 56$, $p\approx1.00$), or nightmare severity ($F=2.80$, $df=1, 56$, $p=0.10$). When adjusted for pretreatment scores by analysis of covariance, posttreatment scores on the Clinician Administered PTSD Scale ($F=0.06$, $df=1, 55$, $d=0.14$, $p=0.81$) and scores for nightmare severity ($F=1.92$, $df=1, 55$, $d=0.37$, $p=0.17$) were nonsignificantly higher (worse) in the treatment group than in the placebo group, and scores on the Pittsburgh Sleep Quality Index showed marginally poorer sleep in the treatment group than in the placebo group ($F=3.68$, $df=1, 55$, $d=0.58$, $p=0.06$). Cyproheptadine serum levels (determined by gas chromatography/mass spectrometry) were available at one site for 14 of 15 treated subjects. Partial correlation analysis, controlling for pretreatment scores, showed a marginally significant correlation of higher cyproheptadine levels with a worsening of Pittsburgh Sleep Quality Index scores ($r=0.47$, $p=0.051$) but no significant correlation with scores on the Clinician Administered PTSD Scale ($r=0.21$, $p=0.25$) or scores for nightmare severity ($r=0.24$, $p=0.22$) (in one-tailed tests).

Contrary to expectation (1, 2), cyproheptadine does not appear to be an effective treatment for sleep problems or combat-related PTSD and may even exacerbate sleep disturbance. Although the study group was relatively small, low power is an unlikely explanation for our nonsignificant findings because of the trend for poorer sleep in the treatment group and the likely correlation of cyproheptadine levels with worsening of sleep. Our results reinforce the need for skepticism about open-label or anecdotal findings and for careful scientific trials to replicate uncontrolled studies.

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Weight Gain With Anorexia Nervosa

TO THE EDITOR: Because of limitations in treatment resources, patients with anorexia nervosa are often asked to gain weight in intensive outpatient programs rather than in traditional inpatient treatment settings. Little is known about the efficacy of intensive outpatient treatment for weight gain in patients with anorexia nervosa.

Using a retrospective chart review of patients with anorexia nervosa, we matched 23 inpatients and 23 patients in intensive outpatient treatment by diagnosis and age, comparing admission and discharge weights, lengths of stay, and rates of weight gain. The inpatient and outpatient groups did not differ significantly on age, age at onset of eating disorder, or duration of illness. The inpatient group weighed significantly less at admission than the outpatient group (mean percent of ideal body weight=71%, SD=9, versus mean=80%, SD=6) ($t=-4.0$, $df=44$, $p<0.0001$). However, the inpatients gained 15% of their ideal body weight during 46 days (SD=27) of hospitalization, at a rate of 0.3% of ideal body weight per day. By comparison, the patients in intensive outpatient treatment gained only 1.4% of ideal body weight during 69 days (SD=45) of treatment, at a rate of 0.01% of ideal body weight per day (difference in weight gain: $t=5.9$, $df=44$, $p<0.0001$).

There was a linear relationship between weight gain and length of stay for the inpatients ($r=0.77$, $p=0.0001$) but not for the outpatients ($r=-0.07$, n.s.). In fact, only seven of the 23 outpatients showed a gain of more than 5% of ideal body weight during treatment. The remaining 16 outpatients showed little weight gain or even lost weight during treatment. Moreover, the outpatients who successfully gained weight all did so at a lower rate than the inpatient group with the lowest percentage weight gain. The subgroups of outpatients and inpatients who gained weight did not differ significantly from the outpatients and inpatients who did not gain weight on any pretreatment variable.

In summary, subjects gained significantly more weight at a faster rate during inpatient treatment than during intensive outpatient treatment. Intensive outpatient treatment was less effective in promoting weight gain and thus may be more expensive over time. It is important to note that the inpatients were supervised during 35 meals a week, whereas the outpatients were supervised for three to 13 meals a week. It is well known that people with anorexia nervosa are resistant to eating a normal number of calories, not to mention gaining weight. Underweight patients with eating disorders tend to eat little during unsupervised meals; this is likely to account for the large differences in weight gain between the outpatient and inpatient groups.

The patients receiving intensive outpatient treatment who gained weight did so at a rate similar to that reported by the Toronto Hospital partial-hospitalization eating disorder programs (1, 2). We are not aware of other studies comparing weight gain in inpatients and outpatients with anorexia nervosa in intensive treatment. However, a number of clinical centers have informally reported similar frustration in trying to promote weight gain in intensive outpatient programs, as reported on an e-mail chat line of the Academy for Eating Disorders.

Further research on the efficacy of eating disorder treatment programs in restoring weight in patients with anorexia nervosa is greatly needed. On the basis of our findings, such studies are likely to show that, in the long run, inpatient treatment is more cost-effective than intensive outpatient treatment for restoring weight in underweight patients with anorexia nervosa.

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Rapid-Cycling Bipolar Disorder in Children

TO THE EDITOR: There has recently been an increase in the number of reports focusing on pediatric bipolarity. An issue of current debate is whether there are presentations of this condition that are unique to youths (1). The retrospective life charting method (2) has been used to describe the longitudinal history of bipolar disorder in adults. We are not aware of any published cases that have utilized this technique in children.

We gave the retrospective life charts to parents of youngsters seen at our institution who met the DSM-IV criteria for bipolar disorder type I to assess the longitudinal course of pediatric bipolarity. Specifically, we wished to ascertain whether pediatric bipolar disorder is a cyclic condition. These procedures were approved by the institutional review board of the University Hospitals of Cleveland. All guardians provided written informed consent, and all patients provided assent before participation.

The parents of 10 outpatients who met the full DSM-IV criteria for a lifetime diagnosis of bipolar disorder type I were instructed on how to complete retrospective life charts, and the parents of each child were given a life chart to complete for their child. These patients' mean age was 12.1 years (range=8–17). Six of these youths were boys. Through the retrospective life charts, the parents of each child described a cyclic, biphasic course in which periods of both mania and depression were present. Seven youths experienced rapid cycling.

In the year before assessment, eight patients had continuous cycling. During this time, the mood episodes were too numerous to count in three of these children. The seven other